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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/553,108

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Nobuo Mochizuki

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DARBY & DARBY P.C.

P.O. BOX 770

Church Street Station

New York, NY 10008-0770

EXAMINER

HAVLIN, ROBERT H

ART UNIT

PAPER NUMBER

1626

MAIL DATE

DELIVERY MODE

01/07/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/553,108	Applicant(s) MOCHIZUKI ET AL.	
	Examiner ROBERT HAVLIN	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 October 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) 4 and 7-12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 5, 6, 13 and 14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the claims: Claims 1-14 are currently pending. Claims 4, and 7-12 are withdrawn.

Priority: This application is a 371 of PCT/JP04/05237 04/13/2004 and claims foreign priority to JAPAN 2003-109667 (04/14/2003) and JAPAN 2004-023032 (01/30/2004).

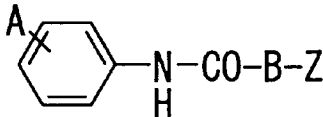
Declarations: The declaration under 37 CFR 1.132 filed 9/24/2008 is found persuasive as to the unexpected result of compound 37. A 55% versus a 19% inhibition is a sufficiently large enough increase that one of ordinary skill in the art would not expect such a change in activity based upon the otherwise obvious structural differences.

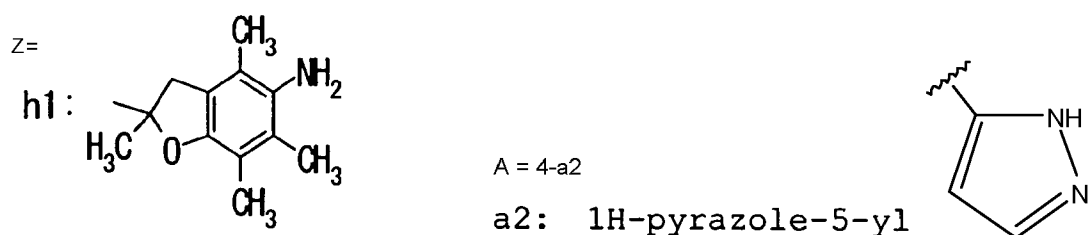
RCE: A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/24/08 has been entered.

Election/Restrictions

1. Applicant previously elected Group I (claims 1-3, 5, 6, and 13) in the reply filed on 9/19/07.

Applicant also elected the following species and claims 1-3, 5, 6, 13, 14 read thereupon:

Compound 37 which is described in Table 1 as: , wherein the variables are defined: A is 4-a2; B is -; and Z is h1. These variables are further defined such that:



As detailed below, the elected species was unpatentable and in accordance with the election of species practice described in the requirement for restriction, subject matter not reading on the elected species is hereby withdrawn.

RESPONSE TO APPLICANT ARGUMENTS

Claim Rejections - 35 USC § 103

2. Claims 1-3, 5, 6, 13, and 14 were rejected under 35 U.S.C. 103(a) as being unpatentable over Umeda et al. (US 6,342,516 or "516" patent) in view of Hansch et al. (Substituent Constants for Correlation Analysis in Chemistry and Biology, (1979), Wiley, pages 1-63). As described above, the 132 declaration showing unexpected results was found persuasive. **Therefore this rejection is withdrawn.**

Claim Rejections - 35 USC § 112

3. Claim 14 was rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Applicant has amended the claims thereby obviating the rejection. **This rejection is withdrawn.**

NEW REJECTIONS / OBJECTIONS

Claim Objections

4. Claims 2, 6, 13 and 14 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 1 defines the scope of "Z" as follows:

Z represents a chroman-2-yl group which is substituted by G2, a 2,3-dihydrobenzofuran-2-yl group which is substituted by G2, a thiochroman-2-yl group which is substituted by G2, a 2,3-dihydrobenzothiophene-2-yl group which is substituted by G2, or a 1,3-benzoxathiol-2-yl group which is substituted by G2,

And does not provide for substitutions other than G2 on the various ring groups listed above. Therefore, definitions in dependent claims providing for a broader scope of substitutions, for example including R7-R17, fail to further limit and are improper.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-3, 5, 6, and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Several of the claims have definitions or use claim language precluding one of ordinary skill in the art from discerning the claim scope. Exemplary language is as follows:

- Claim 1:
 - The claim states: “A represents ... respresented by the following formulae:” but no formulae are provided.
 - The phrases “which may be substituted,” and “which may have a substituent,” are open ended and one of ordinary skill in the art could not determine the metes and bounds of the claim.
- Claim 2:
 - “z” is used when it appears “Z” is intended.
 - The phrase “which may have a substituent,” is open ended and one of ordinary skill in the art could not determine the metes and bounds of the claim.
- Claims 3 and 14:
 - The following language does not logically describe any scope because there is no benzene ring relevant to the context: “which is substituted at the fourth position on the benzene ring.”
- Claims 5 and 6:
 - The phrases “which may be substituted,” and “which may have a substituent,” are open ended and one of ordinary skill in the art could not determine the metes and bounds of the claim.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148

USPQ 459 (1966), that are applied for establishing a background for determining

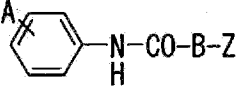
obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

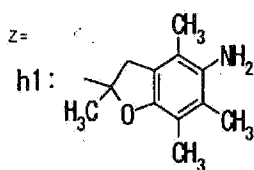
9. Claims 1-3, 5, 6, 13, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,342,516 ('516) in view of Patani et al. (Chem. Rev., 1996, Vol. 96, No. 8, P. 3147-3176).

The instant claims read on the elected species as follows:

Compound 37 which is described in Table 1 as:

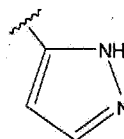


, wherein the variables are defines: A is 4-a2; B is -; and Z is h1. These variables are further defined such that:



A = 4-a2

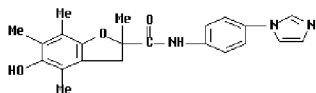
a2: 1H-pyrazole-5-yl



The claim scope also provides for A as imidazolyl. The compounds are useful as antioxidants.

1. Determining the scope and contents of the prior art.

'516 teaches the compound 3-9 in table 3 in column 59:



As a pharmaceutical agent for preventing peroxidized lipid production (col. 2, line 25) and also have antioxidation activity (col. 66, line 4).

Patani et al. teaches on pages 3152-54 the bioisosteric replacement of a hydroxyl group with an amino group while retaining activity. The reference teaches the application generally and also provides several specific examples in related contexts.

2. Ascertaining the differences between the prior art and the claims at issue.

The difference between the '516 compound and the elected species is a hydroxyl instead of an amino substitution at the 5-position of the "h1" group and "A" is an imidazol-1-yl group instead of a pyrazol-5-yl group.

The difference between the claim scope and the '516 compound is only a hydroxyl instead of an amino substitution at the 5-position of the "h1" group.

3. Resolving the level of ordinary skill in the pertinent art.

One of ordinary skill in the art would be well versed in the well-known method of bioisosteric replacement to optimize pharmaceutical compounds. In addition, modifying the 5-position substituent on the "h1" group and modifying an imidazol-1-yl group to a pyrazol-5-yl group is a routine procedure well within the technical grasp of those of ordinary skill in the art.

4. Considering objective evidence present in the application.

One of ordinary skill in the art, upon reading the teaching of '516, immediately recognize through structural similarity and specifically the teaching of Patani that the '516 compound would maintain antioxidant activity if the hydroxyl group were modified to an amino group. Similarly, one of ordinary skill in the art would know that the pyraxol-5-yl isomeric form of the '516 compound would also have the same activity because positional and ring isomers predictably have the same activity. See MPEP 2144.09(II). In *Eisai Co. Ltd. v. Dr. Reddy's Laboratories Ltd.*, 87 USPQ2d 1452, 1454 (Fed. Cir. 2008), the Federal Circuit clarified the proof of obviousness in structural similarity situations such as this:

Where, as here, the patent at issue claims a chemical compound, the analysis of the third Graham factor (the differences between the claimed invention and the prior art) often turns on the structural similarities and differences between the claimed compound and the prior art compounds. See *Eli Lilly & Co. v. Zenith Goldline Pharms., Inc.*, 471 F.3d 1369, 1377 [81 USPQ2d 1324] (Fed. Cir. 2006) (noting that, for a chemical compound, a prima facie case of obviousness requires "structural similarity between claimed and prior art subject matter ... where the prior art gives reason or motivation to make the claimed compositions" (quoting *In re Dillon*, 919 F.2d 688, 692 (Fed. Cir. 1990) (en banc))).

Obviousness based on structural similarity thus can be proved by identification of some motivation that would have led one of ordinary skill in the art to select and then modify a known compound (i.e. a lead compound) in a particular way to achieve the claimed compound. See *Takeda Chem. Indus. v. Alphapharm Pty.*,

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Ltd., 492 F.3d 1350, 1356 [83 USPQ2d 1169] (Fed. Cir. 2007). In keeping with the flexible nature of the obviousness inquiry, KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727, 1739 [82 USPQ2d 1385] (2007), the requisite motivation can come from any number of sources and need not necessarily be explicit in the art. See Aventis Pharma Deutschland GmbH v. Lupin, Ltd., 499 F.3d 1293, 1301 [84 USPQ2d 1198] (Fed. Cir. 2007). Rather "it is sufficient to show that the claimed and prior art compounds possess a 'sufficiently close relationship ... to create an expectation,' in light of the totality of the prior art, that the new compound will have 'similar properties' to the old." Id. (quoting Dillon, 919 F.2d at 692).

Therefore, because the prior art compound possesses a sufficiently close structural relationship to the instantly claimed compounds and Patani further suggests the compound will maintain activity with the specific modification, the claims are obvious.

Claim Objections

Claims 1-14 are also objected to for reading on subject matter outside of the restricted group. No generic claim was held allowable, the claims are restricted to the elected species only and the remaining subject matter held withdrawn.

Conclusion

No claims are in condition for allowance.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT HAVLIN whose telephone number is

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(571)272-9066. The examiner can normally be reached on Mon. - Fri., 7:30am-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful the examiner's supervisor, Joe McKane can be reached at (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert Havlin/
Examiner, Art Unit 1626

/Rebecca L Anderson/
Primary Examiner, Art Unit 1626